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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,866	07/02/2002	Michael Schirner	SCH 1869	6769

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EXAMINER	
HUFF, SHEELA JITENDRA	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 06/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,866	SCHIRNER ET AL.	
	Examiner	Art Unit	
	Sheela J. Huff	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 5/1/06 has been considered and is persuasive-in-part.

Claims 15-34 are pending.

Response to Arguments

Claim Rejections - 35 USC § 112

Claim 16 remains rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The reasons for this rejection are of record in the paper mailed 2/1/06.

Applicant argues that both L19 and E1 are known and available because the sequences of both are known. Applicant further cites Pini et al. for proof. A copy of this reference was not found.

Claims 15-34 remain/are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The reasons for this rejection are of record in

the paper mailed 9/1/05. Please note: The part of the rejection pertaining to claims 26 and 31 is withdrawn in view of applicant's amendment.

Applicant amended the specification and claim to state that Y is =C(CH3)2 and cites Example 1 in the specification for support. It is not clear if the compound recited in Example 1 reads on Y being =C(CH3)2. If applicant believes that the compound in example 1 contains this structure, then applicant is invited to show this using structures.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15-25, 27-30 and 32-33 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Neri et al Nature Biotechnology Vol. 15 p. 1271 (11/97) in view of Viti et al Cancer Research vol. 59 p. 347 (1/99), applicant's admission in the sentence briding pages 7-8 of the specification and Licha et al US 6083485 (filed 11/7/97). This rejection has been modified to include antibody E1. The reasons for this rejection are of record in the paper mailed 2/1/06.

Applicant argues that those skilled in the art would not reasonably expect L19 when in conjugate form with the cyanine dyes to behave in the same manner as unconjugated L19. Applicant argues that there are too many unknowns. Applicant only asserts that there are "unknowns" and has not provided any objective evidence to that immunoconjugates containing dye behave differently from the antibody alone. Neri et al clearly show that the cyanine dye does not effect the binding ability of the scFv, On page 1273, first column, third and fourth full paragraphs and in Figure 3, the references shows a comparison of immunohistochemical staining of cross sections of mice injected

with scFv and mice injected with Cy3 labeled scFv. Both show the same results. Thus, the dye did not change the binding ability of the antibody fragment.

Claims 15-25, 27-30 and 32-33 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Neri et al WO 99/58570 (published 11/18/99) in view of applicant's admission in the sentence bridging pages 7-8 of the specification and Licha et al US 6083485 (filed 11/7/97). Applicant should note that the WO was filed between the filing date of the foreign priority document and the PCT. A perfected copy of the foreign document may help overcome this rejection. The reasons for this rejection are of record in the paper mailed 2/1/06.

Applicant states that a verified translation was attached to the response. No document was found.

Specification

The amendment filed 5/1/06 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the amendment starting at page 11, line 3. Applicant amended the specification to state that Y is =C(CH3)2 and cites Example 1 in the specification for support. It is not clear if the compound recited in Example 1 reads on Y being =C(CH3)2. If applicant believes that the compound in

example 1 contains this structure, then applicant is invited to show this using structures.

Applicant is required to cancel the new matter in the reply to this Office Action.

New Grounds of Rejection

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 23-33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 8-29 of copending Application No. 11/185025. Although the conflicting claims are not identical, they are not patentably distinct from each other because the only difference between the two sets of claims is the scope. Specifically, both sets of claims are directed to methods of using a conjugate for diagnosis. The conjugate in the instant case is

narrower is scope than that of '025 because the conjugate in the instant application is limited to an antibody linked to a cyanine dye, whereas in '025 the conjugate is a protein, peptide, nucleic acid etc linked to the cyanine dye.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 23-33 are directed to an invention not patentably distinct from claims 1-5 and 8-29 of commonly assigned 11/185025. The reasons are set forth above..

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 11/185025, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Claim Rejections - 35 USC § 103

Claims 15-25, 27-30 and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neri et al Nature Biotechnology Vol. 15 p. 1271 (11/97) in view of Viti et al Cancer Research vol. 59 p. 347 (1/99), applicant's admission in the sentence briding pages 7-8 of the specification and Licha et al US 6083485 (filed 11/7/97) and Licha et al 6630570 (filed 4/12/99).

Neri et al discloses making and using scFv(CGS-1) labeled with infrared fluorophore CY and the use of this antibody-dye conjugate to detect blood vessels and to image tumors (reads on using in a pharmaceutical composition) in tumors by fluoresce microscopy (see page 1272 and 1273). ScFv is directed to ED-B fibronectin, which as is also known as oncofetal fibronectin (see abstract).

The only difference between the instant invention and the reference is the cyanine dyes and the use of L19 or E1.

Viti et al discloses that antibody L19 and E1 can be used in vivo to target new forming blood vessels of F9 teratocarcimona(page 349 (second column)) and that these antibodies have increased binding affinity.

Licha et al ('485) disclose a protein-dye conjugate wherein the dye is "F" (col. 4-5) and the a cyanine dye of the formula IIa. This formula reads on applicant's formula in claim 15. The dyes of this reference are irradiated with light from the visible to near infrared range from 650-1200 nm (see abstract and claims and column 8, lines 42-50).

Licha et al ('570) disclose a peptide-dye conjugate wherein the dye is "A1 or A2" (col. 3-4) and the a cyanine dye of the formula II. This formula reads on applicant's formula in claim 15. Specifically, this reference discloses the cyanine dye of claim 34 (see Figure 1).

Additionally in the sentence bridging pages 7-8 of the specification, applicant admits that "both macroscopic and microscopic detection are possible" using dyes in the near infrared range.

Since Licha et al discloses protein/peptide-dye conjugates using cyanine dyes and the use of these dyes in in vivo diagnostics, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use the dyes of the secondary reference in place of the dyes of the primary reference with the expected benefit of achieving a conjugate that can be used in vivo diagnostic assays and with the expected benefit that the conjugate "accumulates in the edge area of the cell tissue of a focus of disease" making the edge area of the focus of disease optically detectable. In view of the fact that L19 and E1 can target newly formed blood vessels (reads on the edge area) in vivo and have increased binding affinity, it also would have been obvious to use L19 or E1 in the conjugate of the primary reference with the expected benefit of achieving an antibody-dye conjugate with higher binding affinity. Since both macroscopic and microscopic detection are possible using dyes in the near infrared range it also would have been obvious to use either detection method when using the protein/peptide-dye conjugates.

Claims 15-25, 27-30 and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neri et al WO 99/58570 (published 11/18/99) in view of applicant's admission in the sentence bridging pages 7-8 of the specification and Licha et al US 6083485 (filed 11/7/97) and Licha et al US 6630570 (filed 4/12/99). Applicant should note that the WO was filed between the filing date of the foreign priority document and the PCT. A perfected copy of the foreign document may help overcome this rejection.

Neri et al discloses making and using monoclonal antibody L19 chemically coupled to the red fluorophore Cy5 and that this conjugate targets ocular angiogenesis in vivo and subsequent ex vivo immunofluorescent microscopic analysis disclose that the localization was around the vascular structures (page 22, lines 15+). The reference also discloses that the L19 antibody localizes to newly formed blood vessels and that the new ocular vessels can be distinguished from the pre-existing ones using L19 (page 9, lines 18+). This reference also discloses that antibody E1 is the antibody that L19 was derived from.

The only difference between the instant invention and the reference is the cyanine dyes.

Licha et al disclose a protein-dye conjugate wherein the dye is "F" (col. 4-5) and the a cyanine dye of the formula IIa. This formula reads on applicant's formula in claim 15. The dyes of this reference are irradiated with light from the visible to near infrared range from 650-1200 nm (see abstract and claims and column 8, lines 42-50).

Licha et al ('570) disclose a peptide-dye conjugate wherein the dye is "A1 or A2" (col. 3-4) and the a cyanine dye of the formula II. This formula reads on applicant's

formula in claim 15. Specifically, this reference discloses the cyanine dye of claim 34 (see Figure 1).

Additionally in the sentence bridging pages 7-8 of the specification, applicant admits that "both macroscopic and microscopic detection are possible" using dyes in the near infrared range.

Since Licha et al discloses protein/peptide-dye conjugates using cyanine dyes and the use of these dyes in in vivo diagnostics, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use the dyes of the secondary reference in place of the dyes of the primary reference with the expected benefit of achieving a conjugate that can be used in vivo diagnostic assays. Because the conjugate would specifically bind to newly formed vessels and not pre-existing ones, this reads on recognizing the edge of the vessel. In view of the fact that L19 is derived from E1 and since L19 can target newly formed blood vessels in vivo, it also would have been obvious to use L19 or E1 in the conjugate of the primary reference. Since both macroscopic and microscopic detection are possible using dyes in the near infrared range it also would have been obvious to use either detection method when using the protein/peptide-dye conjugates.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is 571-272-0834. The examiner can normally be reached on Tuesdays and Thursdays from 5:30am to 2:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheela J Huff
Primary Examiner
Art Unit 1643

sjh